Remarks

I. Amendments

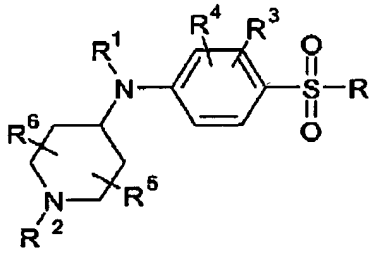
Applicants submit that no further amendment is required.

II. Rejections Under §102

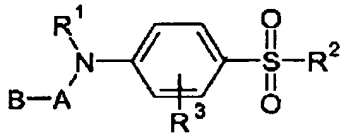
A. Asberom et al.

Claims 1-19 and 28-43 were rejected as anticipated under §102(b) over Asberom et al., WO98/01425. Applicants respectfully traverse.

The compounds disclosed by Asberom et al. are not within Applicants' claims. Please note that the compound cited (formula If at page 7) lacks a substituent corresponding to "A" in Applicants' formula.



Asberom et al. (flipped and rotated for comparison)



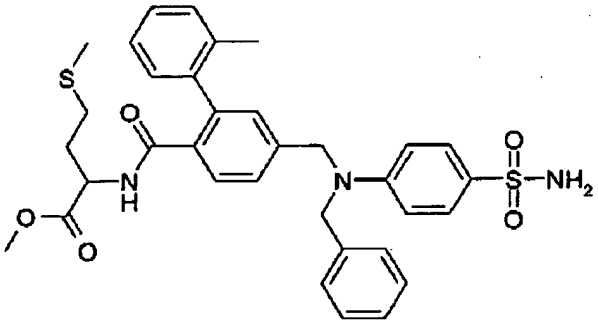
Applicants' claim 1

In Applicant's broadest claim, A is $-(CR_2)_n-$, where n is 1, 2 or 3. Because n cannot be 0, a compound must have at least one methylene group between the anilinic nitrogen and a substituent such as a heterocycle. Thus, Asberom fails to anticipate the present claims. Applicants submit that the rejection of claims 28-37 is moot, because said claims have been canceled.

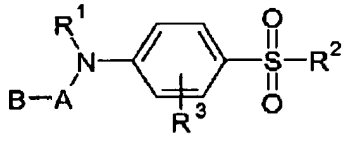
B. Sebti et al., WO98/50029

Claims 1-19 and 28-43 were rejected as anticipated under §102(b) over Sebti et al., WO98/50029. Applicants respectfully traverse.

The compounds cited in Sebti et al. differ substantially from the compounds within Applicants' claim 1.



Example 999A, Sebti et al.



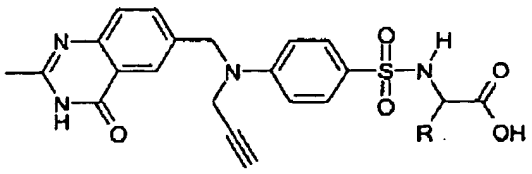
Applicants' claim 1

Although the benzyl substituent may fit within either of Applicants' R^1 or "B–A" substituents, the same is not true for the other group. "B" may be substituted aryl, and the aryl may be substituted with a substituent of the form $-(CR'R'')_n-CONR^aR^b$ (where n can be 0), the substituents R^a and R^b do not include either thioethers or carbonyl derivatives. Thus, the cited Sebti compounds fail to fall within the scope of Applicants' claims, and fail to anticipate said claims. Applicants submit that the rejection of claims 28-37 is moot, because said claims have been canceled.

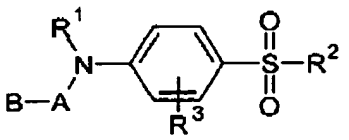
C. Balinska et al.

Claims 1-19 and 28-43 were rejected as anticipated under §102(b) over Balinska et al., *Anticancer Res* (1997) 17:4519-24. Applicants respectfully traverse.

Balinska et al. disclosed compounds taught to have thymidylate synthase inhibiting activity. These compounds, however, differ in structure from Applicants' claimed compounds:



(where R is H or $CH_2CH_2CO_2H$)



Balinska et al. Applicants' claim 1

Note that in Applicants' claim 1 neither R^1 nor B includes an alkynyl substituent. Thus, the compounds disclosed by Balinska et al. fail to anticipate the present claims. Applicants submit that the rejection of claims 28-37 is moot, because said claims have been canceled.

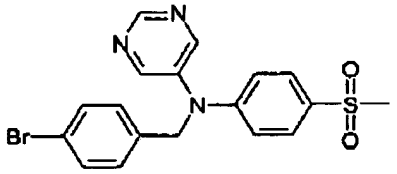
D. Balinska et al.

Claims 1-19 and 28-43 were rejected as anticipated under §102(b) over Balinska et al., *Acta Biochimica Polonica* (1997) 44:743-50. Applicants respectfully traverse.

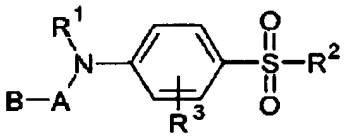
Balinska et al., *Acta Biochimica Polonica* disclosed the same two compounds that were disclosed in Balinska et al., *Anticancer Res* (1997) 17:4519-24 (part C above). As discussed above in part C, these compounds do not fall within the scope of Applicants' claims, and thus fail to anticipate. Applicants submit that the rejection of claims 28-37 is moot, because said claims have been canceled.

E. Okada et al.

Claims 1-19 and 28-43 were rejected as anticipated under §102(b) over Okada et al., *Chem Pharm Bull* (1997) 45(8):1293-99. Applicants respectfully traverse.



Okada et al.



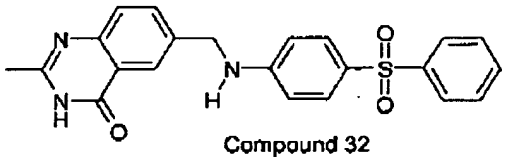
Applicants' claim 1

This compound also fails to fall within Applicants' claims due to the pyrimidinyl group. Applicants' R^1 substituent may be aryl, heteroaralkyl, heterocyclyl, etc., but does not include heteroaryl. Note that "aryl" as defined in Applicants' specification (see p. 4, lines 7-18) does not include heteroaryl, and that "heterocyclyl" is specifically defined as non-aromatic (see p. 6, lines 14-29). R^1 may also be heteroaralkyl, but the compound disclosed in Okada et al. lacks the alkylene linkage. Thus, the

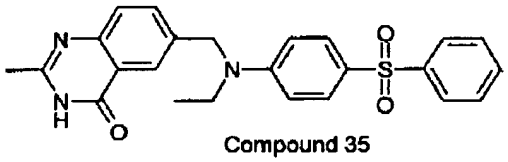
compound disclosed fails to fall within Applicants' claims, and fails to anticipate. Applicants submit that the rejection of claims 28-37 is moot, because said claims have been canceled.

F. Jones et al.

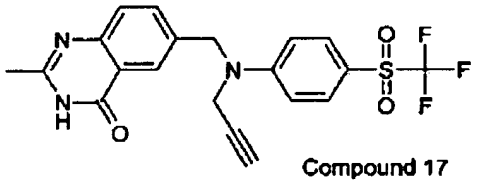
Claims 1-19 and 28-43 were rejected as anticipated under §102(b) over Jones et al., *J Med Chem* (1996) 39:904-17. Applicants respectfully traverse.



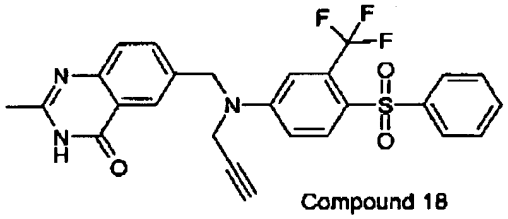
Compound 32



Compound 35

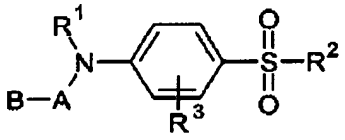


Compound 17



Compound 18

Jones et al.



Applicants' claim 1

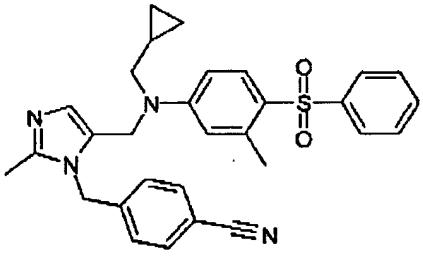
As discussed above with respect to Balinska et al., Applicants' claims do not include compounds in which either R^1 or B–A can be alkynyl: further, neither R^1 nor B–A can be simply H. Thus, compounds 17, 18, and 32 are excluded from Applicants' claims.

Compound 35 (wherein R^1 is ethyl) also fails to fit. Substituent B may be heteroaryl, but heteroaryl is limited in claim 1 to furyl, imidazolyl, pyridyl, thienyl, thiazolyl, benzothiazolyl, and

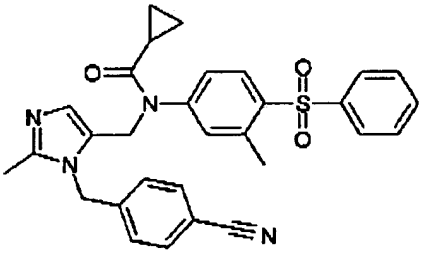
pyridazinyl. Thus, none of the cited compounds fall within Applicants' claims, and thus fail to anticipate. Applicants submit that the rejection of claims 28-37 is moot, because said claims have been canceled.

G. Dinsmore et al.

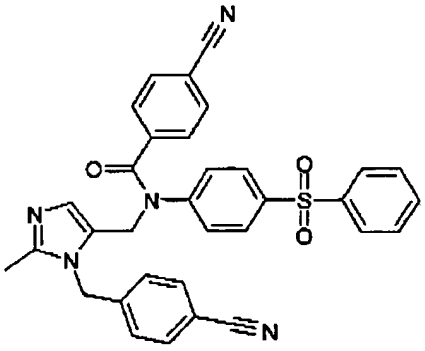
Claims 1-19 and 28-43 were rejected as anticipated under §102(b) over Dinsmore et al., *Bioorg Med Chem Lett* (1999) 9:3301-06. Applicants respectfully traverse.



Compound 8e

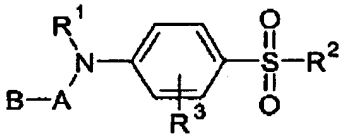


Compound 8f



Compound 8g

Dinsmore et al.



Applicants' claim 1

The Dinsmore et al. compounds differ from the claimed compounds in that they include heteroaryl substituted with arylalkyl substituents, which are not included in Applicants' claims. Note that when "B" is heteroaryl in claim 1, the substituents with which heteroaryl may be optionally substituted do not include either aryl or aralkyl. Accordingly, Dinsmore fails to anticipate Applicants' claims. Applicants submit that the rejection of claims 28-37 is moot, because said claims have been canceled.

III. Rejections Under §103

A. Asberom et al.

Claims 1-19 and 28-43 were rejected as obvious under §103(a) over Asberom et al., WO98/01425. Applicants respectfully traverse.

As discussed in part II.A. above, Asberom et al. does not actually disclose compounds within the scope of the present invention. Applicants can find no suggestion in the cited reference to modify the compounds therein in such a way as to arrive at the compounds of the present invention. Thus, Applicants respectfully submit that a prima facie case of obviousness has not been established.

Applicants submit that the rejection of claims 28-37 is moot, because said claims have been canceled.

B. Sebti et al., WO98/50029

Claims 1-19 and 28-43 were rejected as obvious under §103(a) over Sebti et al., WO98/50029. Applicants respectfully traverse.

As discussed in part II.B. above, Sebti et al. does not actually disclose compounds within the scope of the present invention. Applicants can find no suggestion in the cited reference to modify the compounds therein in such a way as to arrive at the compounds of the present invention. Thus, Applicants respectfully submit that a prima facie case of obviousness has not been established.

Applicants submit that the rejection of claims 28-37 is moot, because said claims have been canceled.

C. Balinska et al.

Claims 1-19 and 28-43 were rejected as obvious under §103(a) over Balinska et al., *Anticancer Res* (1997) **17**:4519-24. Applicants respectfully traverse.

As discussed in part II.C. above, Balinska et al. does not actually disclose compounds within the scope of the present invention. Applicants can find no suggestion in the cited reference to modify the compounds therein in such a way as to arrive at the compounds of the present invention. Thus, Applicants respectfully submit that a prima facie case of obviousness has not been established.

Applicants submit that the rejection of claims 28-37 is moot, because said claims have been canceled.

D. Balinska et al.

Claims 1-19 and 28-43 were rejected as obvious under §103(a) over Balinska et al., *Acta Biochimica Polonica* (1997) 44:743-50. Applicants respectfully traverse.

As discussed in part II.D. above, Balinska et al. does not actually disclose compounds within the scope of the present invention. Applicants can find no suggestion in the cited reference to modify the compounds therein in such a way as to arrive at the compounds of the present invention. Thus, Applicants respectfully submit that a prima facie case of obviousness has not been established.

Applicants submit that the rejection of claims 28-37 is moot, because said claims have been canceled.

E. Okada et al.

Claims 1-19 and 28-43 were rejected as obvious under §103(a) over Okada et al., *Chem Pharm Bull* (1997) **45(8)**:1293-99. Applicants respectfully traverse.

As discussed in part II.E. above, Okada et al. does not actually disclose compounds within the scope of the present invention. Applicants can find no suggestion in the cited reference to modify the compounds therein in such a way as to arrive at the compounds of the present invention.

Thus, Applicants respectfully submit that a prima facie case of obviousness has not been established.

Applicants submit that the rejection of claims 28-37 is moot, because said claims have been canceled.

F. Jones et al.

Claims 1-19 and 28-43 were rejected as obvious under §103(a) over Jones et al., *J Med Chem* (1996) 39:904-17. Applicants respectfully traverse.

As discussed in part II.F. above, Okada et al. does not actually disclose compounds within the scope of the present invention. Applicants can find no suggestion in the cited reference to modify the compounds therein in such a way as to arrive at the compounds of the present invention. Thus, Applicants respectfully submit that a prima facie case of obviousness has not been established.

Applicants submit that the rejection of claims 28-37 is moot, because said claims have been canceled.

G. Dinsmore et al.

Claims 1-19 and 28-43 were rejected as obvious under §103(a) over Dinsmore et al., *Bioorg Med Chem Lett* (1999) 9:3301-06. Applicants respectfully traverse.

As discussed in part II.G. above, Dinsmore et al. does not actually disclose compounds within the scope of the present invention. Applicants can find no suggestion in the cited reference to modify the compounds therein in such a way as to arrive at the compounds of the present invention. Thus, Applicants respectfully submit that a prima facie case of obviousness has not been established.

Applicants submit that the rejection of claims 28-37 is moot, because said claims have been canceled.

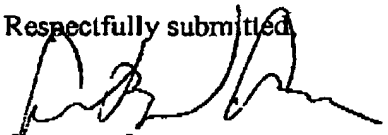
To establish a prima facie case of obviousness under §103(a), the Office must point to statements in the art that would suggest or teach the claimed invention to one of ordinary skill in the art.

Applicants fail to see any such teaching in the cited references. Asberom et al. teaches compounds alleged to be useful as muscarinic antagonists. Sebti et al. teaches compounds that are alleged to be useful as inhibitors of protein isoprenyl transferase. Balinska et al. (both references) and Jones et al. teach compounds that are alleged to be useful as inhibitors of thymidylate synthase. Okada et al. teaches compounds that are alleged to be useful as inhibitors of aromatase. Dinsmore et al. teaches compounds that are alleged to be useful as inhibitors of farnesyl-protein transferase. None of the protein targets in the cited references is related in any known way to prostaglandin G/H synthase I or II (COX I and COX II), which are the enzymes inhibited by the compounds of the invention. One of ordinary skill in the art would not expect that modifying a thymidine synthase inhibitor based on the structure of an aromatase inhibitor (or vice versa) would result in any advantageous properties at all, much less a compound having an unrelated activity.

Thus, Applicants submit that no prima facie case of obviousness has been established, or can be established based on the cited references, and that the rejection is thus overcome.

Applicants respectfully submit that the application is now in condition for allowance. Any questions regarding the application may be directed to the undersigned at the telephone or email addresses given below.

Respectfully submitted,



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September 8, 2005

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